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UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

OAKLAND DIVISION

STEPHEN WENDELL AND LISA WENDELL, for themselves and as successors in interest to MAXX WENDELL, DECEASED,

Plaintiffs,

v.

JOHNSON & JOHNSON; CENTOCOR, INC.; ABBOTT LABORATORIES; SMITHKLINE BEECHAM d/b/a GLAXOSMITHKLINE; TEVA PHARMACEUTICALS USA; GATE PHARMACEUTICALS, a division of TEVA PHARMACEUTICALS USA; PAR PHARMACEUTICAL, INC.;

Defendants.

Case No: 4:09-cv-04124-CW

NOTICE OF MOTION AND MOTION TO EXCLUDE TESTIMONY UNDER FEDERAL RULE OF EVIDENCE 702 AND FOR SUMMARY JUDGMENT BY DEFENDANTS ABBOTT LABORATORIES, JOHNSON & JOHNSON, CENTOCOR, INC., AND TEVA PHARMACEUTICALS USA, INC.; MEMORANDUM OF POINTS AND AUTHORITIES IN SUPPORT

Date: February 20, 2014
Time: 2:00 p.m.
Courtroom: Room 2, 4th Floor
1301 Clay Street
Oakland, CA 94612

Judge: Honorable Claudia Wilken

NOTICE OF MOTION AND MOTION TO EXCLUDE TESTIMONY UNDER FEDERAL RULE OF EVIDENCE 702 AND FOR SUMMARY JUDGMENT BY DEFENDANTS ABBOTT LABORATORIES, JOHNSON & JOHNSON, CENTOCOR, INC., AND TEVA PHARMACEUTICALS USA, INC.

TO ALL PARTIES AND THEIR ATTORNEYS OF RECORD:

PLEASE TAKE NOTICE THAT on Thursday, February 20, 2014, at 2:00 p.m., in Courtroom No. 2 of the United States District Court for the Northern District of California, 1301 Clay Street, Oakland, California, 94612, Honorable Claudia Wilken presiding, Defendants Abbott Laboratories ("Abbott"), Johnson & Johnson ("J&J"), Centocor, Inc. ("Centocor") (collectively, "Anti-TNF Defendants"), and Teva Pharmaceuticals USA, Inc. ("Teva") (collectively, "Defendants") will and hereby do move this Court to exclude the testimony of the experts of Stephen Wendell and Lisa Wendell, his wife, for themselves and as successors-in-interest to Maxx Wendell ("Wendell"), deceased (collectively, "Plaintiffs"), under Federal Rule of Evidence 702, and for summary judgment in favor of Defendants under Federal Rule of Civil Procedure 56 on all claims for relief asserted by Plaintiffs against Abbott (First and Second Counts of Plaintiffs' Fourth Amended Complaint ("FAC")); Johnson & Johnson and Centocor (Third and Fourth Counts); and Teva (Fifth and Sixth Counts).

Defendants move for exclusion of Plaintiffs' experts' testimony on the grounds that it is unreliable under *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 589 (1993) ("*Daubert I*") and therefore inadmissible. Defendants move for summary judgment on the grounds that there is no genuine issue as to any material fact related to any of the causes of action against Defendants, all of which are based on a theory of failure to warn. As described further in the accompanying Memorandum of Points and Authorities, Defendants are entitled to summary judgment because Plaintiffs cannot prove essential elements of their failure-to-warn claims—namely, general causation, specific causation, or breach of any duty to warn as to any Defendant, or proximate causation as to Teva.

MEMORANDUM OF POINTS AND AUTHORITIES

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INTRODUCTION

Plaintiffs have undeniably suffered a tragic loss in the death of their son, Maxx Wendell. But this case turns on the law, the facts, and the relevant science. With discovery now complete, Plaintiffs have failed to raise a triable issue of fact for a jury that any of the defendants are responsible for his death for two independent reasons:

First, Plaintiffs cannot establish causation against any Defendant. Plaintiffs' speculative theory that the combined use of Defendants' therapies to treat Wendell's ulcerative colitis (a type of inflammatory bowel disease ("IBD")), somehow caused or contributed to his development of hepatosplenic T-cell lymphoma ("HSTCL") is insufficient as a matter of law. Plaintiffs are required under California law to show that each of Defendants' products was a substantial factor in Wendell's development of HSTCL, by showing that each Defendant's therapy was a but-for cause of Wendell's HSTCL or was independently sufficient to cause his disease. They cannot meet this burden. Plaintiffs' causation experts, Drs. Weisenburger and Shustov, who have testified that over 70% of HSTCL cases have no known cause, admit that they cannot ascribe an individual causal role to *any* of Defendants' individual therapies. They cannot point to *any* scientific support for the claim that the Anti-TNF Defendants' therapies increase the risk of HSTCL either when used alone or when added to thiopurine therapy. And neither expert can point to any scientific evidence that Wendell's very short use of Abbott's Humira immediately before his diagnosis for HSTCL contributed to the development of the disease or, indeed, that it was not already present. Nor can they point to any reliable scientific study demonstrating that Teva's product, Purinethol, increased Wendell's HSTCL risk or caused his HSTCL. Their untested hypothesis that all of these treatments combined in some unknown and undefined way to cause Wendell's disease is purely speculative and inadmissible under Rule 702 and *Daubert*. Because Plaintiffs have no reliable and admissible expert testimony to support their claim that Defendants' therapies cause HSTCL or in fact caused Wendell's HSTCL, Defendants are entitled to summary judgment on all of Plaintiff's claims.

Second, Plaintiffs cannot establish a failure to warn claim against any Defendant. When Wendell's gastroenterologist, Dr. Edward Rich, prescribed Defendants' therapies to treat Wendell's ulcerative colitis, none of Defendants' products were FDA-approved for such treatment. Because

Wendell's use of Defendants' products was thus "off-label," Plaintiffs' failure-to-warn claims cannot stand without proof that Defendants promoted the off-label use and that Wendell's physician, Dr. Edward Rich, relied on that promotion. There is no evidence that any Defendant promoted its product for such use, let alone that Dr. Rich relied on any such overpromotion, so Plaintiffs' failure-to-warn claims against all Defendants fail.

Even apart from the off-label use, Plaintiffs cannot establish that any Defendant had a duty to warn about the potential risk of HSTCL when Wendell was prescribed its product because it is undisputed that not a single case of HSTCL in an IBD patient who had taken Defendants' products had been reported prior to Dr. Rich's prescription of Defendants' products for Wendell. Plaintiffs have no admissible evidence that any Defendant had a duty to warn in these circumstances—only the unsupported *ipse dixit* of their warnings expert, Dr. David Ross. Moreover, Plaintiffs cannot prove proximate cause as to Teva because, among other reasons, it is undisputed that Dr. Rich never even read Teva's label and therefore could not have relied on any alleged lack of warning.

For these reasons, Defendants respectfully move the Court to exclude the testimony of Plaintiffs' causation and warning experts and grant summary judgment to each Defendant on all of Plaintiffs' causes of action.

STATEMENT OF RELEVANT FACTS

I. MAXX WENDELL'S MEDICAL TREATMENT

Maxx Wendell was diagnosed with probable ulcerative colitis in late 1998 at the age of 12. In July 1999, after unsuccessful treatment with steroids, Wendell's physician, Dr. Rich, added Purinethol® (chemical name: 6-MP), a thiopurine, to Wendell's medications. Ex.[1] 1 (Rich Dep.) at 79-82, 105.[2] Dr. Rich's prescription of Purinethol was "off-label' because the drug was not approved to treat IBD. FAC (Dkt. 165) ¶ 47. In May 2002, Dr. Rich began to discuss anti-TNF therapy with Wendell and his family as another treatment option, including its benefits and possible side effects. *Id*. at 117-118, 122-123. In July 2002, Dr. Rich prescribed the anti-TNF Remicade (infliximab) to Wendell in an attempt to

[1] "Ex." Refers to exhibits to the Omnibus Appendix in Support of Motion filed herewith.

[2] Wendell received Purinethol from GlaxoSmithKline ("GSK") initially, Purinethol from Teva between December 16, 2003, and July 27, 2004, and a generic 6-MP product from Par Pharmaceutical, Inc., thereafter. Ex. 13 (pharmacy records disclosed by Plaintiffs) at 2-13.

permanently wean him off steroids. *Id*. 147-48, 151-52. This use was also off-label as Remicade was not approved for the treatment of ulcerative colitis at the time, but only Crohn's disease, a different type of IBD. *See* Ex. 16 (6/28/2002 Remicade label) at 11. Wendell took Remicade in combination with 6-MP through early 2006. *Id*. 177-78.

After a clear colonoscopy in May 2006, Dr. Rich discontinued Wendell's Remicade. *Id*. at 198-99. But after another IBD flare in November 2006, Dr. Rich prescribed Humira. *Id*. at 216-17. The Humira prescription was also off-label because Humira was not approved for the treatment of any type of IBD. *See* Ex. 3 (11/9/2006 Humira Label) at ABT 01614563. Wendell stopped taking 6-MP in, at the latest, April 2007. His last Humira prescription was on June 15, 2007. *See* Ex. 1 at 272-73.

In July 2007, Wendell was diagnosed with HSTCL, a very rare and aggressive form of lymphoma. He passed away on December 6, 2007.

II. FACTS RELEVANT TO CAUSATION

HSTCL was first identified as a specific type of lymphoma in the 1990s. Ex. 4 (Dep. of Dennis Weisenburger, M.D.) at 46. Plaintiffs' two purported causation experts testified that the vast majority of HSTCL cases—at least 73%—are idiopathic, meaning they have no known cause. *Id*. at 174; Ex. 6 (Dep. of Andrei Shustov, M.D.) at 106. Nevertheless, they contend that the combination of 6-MP, Remicade, and Humira caused or substantially contributed to Wendell's HSTCL. Ex. 7 (Weisenburger Rep.) at 2; Ex. 8 (Shustov Rep.) at 13. They do not offer this opinion as to any of Defendants' drugs individually. *See generally* Exs. 7 & 8.

A. Plaintiffs' Experts' Testimony Concerning Anti-TNF Therapies Remicade and Humira

Plaintiffs' experts do not contend that anti-TNFs alone increase HSTCL risk. *See* Ex. 8 at 11-13; Ex. 7 at 2. In fact, both confirmed that they had no opinion that anti-TNF therapies themselves increase HSTCL risk. *See* Ex. 4 (Weis. Dep.) at 100 (no opinion that anti-TNF monotherapy increases HSTCL risk); Ex. 6 (Shustov Dep.) at 107 (could not identify a single case of HSTCL in an IBD patient on anti-TNF monotherapy). Thus, neither expert could say that Wendell developed HSTCL because he took anti-TNF therapy to treat his IBD. *See* Ex. 4 (Weis. Dep.) at 113 (testifying that it was "unlikely" that "Wendell [would] have developed HSTCL if he had only taken Humira as a monotherapy"). Plaintiffs'

experts also admitted that they could not opine that Wendell would not have developed HSTCL had he not taken an anti-TNF therapy. Weisenburger admitted that he could not offer such an opinion with regard to Humira. *See* Ex. 4 at 112 ("Q. And would Mr. Wendell have developed HSTCL if he had never taken Humira? A. We don't know the answer to that."). Likewise, Shustov could not offer an opinion to a reasonable degree of medical certainty about whether Wendell would have developed HSTCL had he not taken Humira, Ex. 6 at 165, or Remicade, *id*. at 234.

Because they do not opine that anti-TNFs themselves increased HSTCL risk or caused Wendell's HSTCL, *see generally* Exs. 4, 6, Plaintiffs' experts speculate that combining such therapies with thiopurine somehow increases the risk. But neither expert could say that adding anti-TNF treatments to Wendell's existing thiopurine treatment regimen increased his risk of HSTCL beyond the risk, if any, from thiopurine treatment. Weisenburger admitted that "*it would be impossible*, based on the data that we have today, *to say whether or not the addition of Humira* to Max[x] Wendell's treatment regimen *increased his risk* of HSTCL." *Id*. at 217 (emphasis added); The same is true for Remicade. *Id*. Shustov similarly testified that he "cannot quantify" the "relative risk" of 6-MP, Remicade, or Humira to Wendell's development of HSTCL. Ex. 6 at 164. He cannot "separate out" the "relative contribution" of Humira in particular to his HSTCL risk. *Id*. at 164-65. Shustov could not even opine to a reasonable degree of medical certainty that the use of Humira when added to Wendell's treatment regimen actually increased his HSTCL risk—he would only state, "I can't quantify the increase in risk. It continued the risk in my opinion." *Id*. at 165-66.

B. Plaintiffs' Experts' Testimony Concerning Mercaptopurine

The facts relevant to Plaintiffs' causation assertions against Teva are included in the Argument section below.

III. FACTS RELEVANT TO WARNINGS

A. Facts Relevant to Plaintiffs' Warnings Claims Against Teva

Dr. Rich testified that he decided to prescribe 6-MP to treat Maxx Wendell based on information he learned during his fellowship, as well as on information he obtained from reading medical articles, from speaking with other professionals in his field, and from "patient experience." Ex. 1 (Rich Dep.) at 274-75. He learned about the use of 6-MP in pediatric patients with IBD during his pediatric

gastroenterology fellowship training. *Id*. at 84. Dr. Rich was in fellowship training from 1989 to 1992. *Id*. at 37-38.

It is not Dr. Rich's regular practice to look at drug labeling and he has no recollection of reading anything about Purinethol written, published, or disseminated by Teva. *Id*. at 192, 283. Dr. Rich does not recall ever being visited by a representative from Teva regarding Purinethol. *Id*. at 20.

B. Facts Related to Remicade Warnings

Centocor timely updated the Remicade label to reflect the evolving scientific knowledge regarding the risk of HSTCL. When first approved to treat Crohn's disease in August 1998, the label warned of the possible risk of malignancies and lymphoma. Aff. of Dr. Jones ("Jones Aff.") (Dkt. 207) ¶ 7. Between 1998 and 2005, Centocor updated the label regarding these possible risks on nine separate occasions. *Id*. at ¶ 8-10; *see also* Exs. 38-42, 47. These updates were in response to case reports and clinical trials data, and included comprehensive reviews in conjunction with the FDA. *See, e.g.*, Exs. 35-36, 43-45. At the time Wendell was first prescribed Remicade in July 2002, the label did not specifically identify HSTCL because Centocor had received no reports of HSTCL in patients who had taken Remicade. Plaintiffs' warnings expert claims the labeling should have been changed in 2002 based on two case reports. *See* Ex. 23 (MedWatch No. 2002025716 ("Case 1"); Ex. 24 (MedWatch No. 2002018092 ("Case 2")). Case 1, which was initially reported as a "T delta gamma lymphoma" and reviewed as a possible HSTCL case in 2006, has never been confirmed to be an HSTCL case. *See* Ex. 17 (Dep. of Suzanne Travers, M.D.) at 97-98, 120; Ex. 18 (Dep. of Robert Diamond) at 112-14. *See also* Ex. 37 (Email from Ann Corken (FDA) to Sharon Popik, March 8, 2007). Case 2 was reported as a "possible lymphoma"; the HSTCL diagnosis was not known by Centocor until May 2006. Ex. 17 at 124-26.

Centocor first learned of an HSTCL case in March 2003 almost a year after Wendell began taking off-label combination therapy. *See* Ex. 25 (MedWatch No. 2003007578 ("Case 3")). Centocor learned of a second HSTCL case in 2004 two years after Wendell began taking off-label combination therapy. *See* Ex. 26 (MedWatch No. 20041005761 ("Case 4")). Cases 3 and 4 were extremely complicated with many concomitant medications and confounding factors present, including the common use of immunomodulators Azathioprine (in Case 3) and 6-MP (in Case 4). *See id*.; Ex. 19

(Thayu 2005). An article was published about Case 4 in a medical journal in 2005. Ex. 19. Thereafter, Centocor contacted the senior author of the article, Dr. Robert Baldassano. Ex. 20 (Baldassano Dep.) at 48-49, 51-52. Dr. Baldassano informed Centocor that it had been very difficult to diagnose HSTCL. *Id*. at 53-54. He learned of the case in 2003, but did not discuss it with anyone at Centocor until late 2005 because he and his colleagues "had no idea how relevant this was to anything….It wasn't one drug – I mean, the child was on six different drugs. She had gotten a large amount of ionizing radiation. We had no idea what might be the cause of her [HSTCL]." *Id*. at 57-58, 63, 68. The initial misdiagnosis of autoimmune hepatitis in Case 4 was later revised by second opinions from Dr. Baldassano and others from a "combination of [medical] centers," including the NIH. *Id*. at 52-54, 79. Moreover, Dr. Baldassano thought that the FDA was already aware of this case because the patient was diagnosed at NIH. *Id*. at 62, 79.

Centocor and the FDA together reviewed possible reports of lymphoma for Remicade, and evaluated the label over time. The first four cases were provided to the FDA in safety submissions between 2002 and 2005. *See* Exs. 29-33 (PSURs), Ex. 34 (Remicade Summary). Cases 5 and 6 were reported as "gamma delta T-Cell lymphoma" in October and December 2005. *See* Ex. 27-28; *see also* Ex. 46 (Summary of MedWatch Reports). Centocor investigated and followed-up each with the FDA, learning of HSTCL in Case 5 in May 2006, and never confirming HSTCL for Case 6. Ex. 17 (Travers Dep.) at 54-55, 143-45.

In May 2006, the FDA approved Remicade for treatment of active pediatric Crohn's disease. *See* May 19, 2006 FDA Remicade approval letter at 1.[3] By this time, there had been reported to the FDA six post-marketing cases of HSTCL in pediatric patients or young adults taking Remicade in conjunction with the thiopurines azathioprine ("AZA") or 6-MP, and the FDA required revision of the Remicade label to add a boxed warning reporting these cases. *See* Ex. 2 (5/19/2006 Remicade label) at 15. Shortly thereafter Remicade's manufacturer, Centocor, distributed a Dear Health Care Professional ("DHCP") letter describing the six cases, five of which were in patients between 12 and 19 years of age.

[3] Available at http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2006/103772s5138ltr.pdf.

See Ex. 14 (Centocor DHCP letter) at 1. It is undisputed that Dr. Rich received this letter. Ex. 1 at 201-02.

C. Facts Relevant to Abbott's Duty to Warn

While anti-TNFs have similarities, they also have differences, and for this reason anti-TNFs are not treated identically from a safety labeling perspective. FDA thus implements "class" warnings for anti-TNFs where appropriate, but recognizes that a potential risk associated with one anti-TNF may not justify a warning for another drug in the class. As Dr. Jeffrey Siegel, the FDA Reviewer who was "intimately involved" with the agency's reviews of anti-TNF therapies, Ex. 10 (Dep. of David Ross, M.D. ("Ross Dep. I")) at 266-67, explained, "[w]here the data [regarding adverse events] is similar, especially where there is a biologic rationale, class labeling may be warranted, but where the data differ, different language may be appropriate for different agents." *Id*. at 267 (discussing Siegel's testimony at March 2003 FDA Advisory Committee meeting regarding anti-TNF therapies).

Humira warned of potential lymphoma risk since it was first approved by FDA in 2002, and in 2004 FDA subsequently implemented class warnings for lymphoma based on Humira's labeling. *See, e.g.*, Ex. 9 (December 31, 2002 Humira Label) at ABT 01614276; *see also* Ex. 10 (Ross Dep. I) at 250, 265. There has never been such class labeling for HSTCL, however, and Humira did not carry an HSTCL warning when Dr. Rich prescribed Humira off label to Wendell in November 2006. As Plaintiffs' warning expert concedes, at that time "Abbott had not received a single report of HSTCL in a patient taking Humira," *id*. at 212, nor were there any reports in the published medical literature of such a case. *Id*. at 214. In fact, Abbott did not receive its first report of HSTCL in an IBD patient who had taken Humira until February 2008, *id*. at 217-18, (long after Wendell became ill) so there was "[n]othing in Abbott's database prior to February of 2008 that would have constituted an HSTCL safety signal," *id*. at 220. Wendell's case, which was reported to Abbott as an HSTCL case in April 2008, was only the second report Abbott received of an HSTCL case in a Humira IBD patient, *id.* at 216, and the only report made to the FDA by that time, *id*. at 216. Shortly after receiving these two reports, Abbott proactively proposed adding an HSTCL warning to its label. *Id*. at 229.

ARGUMENT

I. LEGAL STANDARDS

Under Rule 702, "the trial judge must ensure that any and all scientific testimony or evidence admitted is not only relevant, but reliable." *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 589 (1993) ("*Daubert I*"); *see also Kumho Tire Co., v. Carmichael*, 526 U.S. 137, 149 (1999) (extending *Daubert* to all expert testimony). Plaintiffs bear the burden of proving admissibility. *See, e.g.*, *Messick v. Novartis Pharms. Corp.*, 924 F. Supp. 2d 1099, 1103 (N.D. Cal. 2013). "The court must examine whether [the expert's] opinion has objective, independent validation of his methodology which is scientifically reliable as a basis for such an opinion." *Casey v. Ohio Med. Prods.*, 877 F. Supp. 1380, 1384 (N.D. Cal. 1995). Untested hypotheses are not admissible. *See Henricksen v. ConocoPhillips Co.*, 605 F. Supp. 2d 1142, 1178 (E.D. Wash. 2009) ("Evidence that is an insightful hypothesis is not admissible in court if it lacks scientific rigor" because "the law lags science; it does not lead it.") (citation and quotation marks omitted). "[O]pinion evidence that is connected to existing data only by the *ipse dixit* of the expert" is likewise inadmissible. *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997); *see also* Fed. R. Evid. 702 advisory committee notes (2000 amendments) ("The trial court's gatekeeping function requires more than simply 'taking the expert's word for it.'" (quoting *Daubert II*)).

Summary judgment is required when there is no genuine issue as to any material fact and the moving party is entitled to judgment as a matter of law. Fed. R. Civ. P. 56(c); *Motus v. Pfizer Inc.*, 196 F. Supp. 2d 984, 989 (C.D. Cal. 2001) ("*Motus I*"), *aff'd sub nom. Motus v. Pfizer Inc.*, 358 F.3d 659 (9th Cir. 2004) ("*Motus II*").

II. PLAINTIFFS CANNOT ESTABLISH THAT WENDELL'S TREATMENTS FOR IBD CAUSED HIS HSTCL

A. Plaintiffs Must Prove Causation For Each Of Defendants' Therapies.

"California has definitively adopted the substantial factor test of the Restatement Second of Torts for cause-in-fact determinations." *Viner v. Sweet*, 30 Cal. 4th 1232, 1239 (2003) (quotation and citation omitted). The general rule is the "but for test of causation" of Restatement (Second) § 432 (1965) ("Section 432"), subsection (1). According to that rule, "if the injury would have occurred even if the actor had not acted wrongfully," the actor's "conduct generally cannot be deemed a substantial factor in the harm." *In re Ethan C.*, 54 Cal. 4th 610, 640 (2012).

Subsection (2) of Section 432 provides a limited exception to the but-for rule in circumstances involving "concurrent *independent*" or "multiple *sufficient* causes." *Viner*, 30 Cal. 4th at 1240 (emphasis added). Subsection (2) applies only where "multiple forces[,] operating at the same time and independently," would each "have been sufficient by itself to bring about the harm." *Id*. The commentary to Section 432 provides an illustration: where two fires set by separate negligent acts of different defendants coalesce before burning down plaintiff's house, the negligence of both defendants may be found to be a substantial factor under Subsection (2) ***if*** either fire would have burned down the house had the other not occurred. *See* Section 432, Comment on Subsection (2) (illustration 3).

Critically, under subsection (2), where multiple "forces operated in combination, with none being sufficient in the absence of the others to bring about the harm, they are not concurrent *independent* causes." *Viner*, 30 Cal. 4th at 1240 (emphasis in original). In such a case, "the exception stated in subsection (2) of Restatement section 432 does not apply, and th[e] case is governed by the 'but for' test" stated in Section 432(1). *Id*.[4] In other words, alleging multiple *interdependent* causes does not excuse Plaintiffs from the burden of proving causation. Under Section 432 of the Restatement and California law, they *must* prove that *each* therapy was a but-for or concurrent independent cause of Wendell's HSTCL. This they have not done, and cannot do, as discussed more fully in Sections II.C., D., and E. below.

B. Plaintiffs' Causation Experts' Reports, Developed Solely for Litigation and After Inadequate Preparation, Are Unreliable.

Plaintiffs must establish "within a reasonable medical probability based upon competent expert testimony…that the substance at issue was capable of causing the injury alleged (general causation), and that the substance caused, or was a substantial factor in causing, the specific plaintiff's injury (specific causation)." *Avila v. Willits Envtl. Remediation Trust*, 633 F.3d 828, 836 (9th Cir. 2011) (citations omitted); *see also Jones v. Ortho Pharm. Corp.*, 163 Cal. App. 3d 396, 402 (1985) (in a personal injury action, "causation must be proven within a reasonable medical probability based upon competent expert testimony").

[4] *See also Xavier v. Philip Morris USA Inc.*, 787 F. Supp. 2d 1075, 1080 (N.D. Cal. 2011) (applying *Viner* in products liability case); *Torres v. City of Madera*, 2005 WL 1683736, at *6 (E.D. Cal. July 11, 2005) (same), *aff'd sub nom. Torres v Taser Int'l, Inc.*, 277 F. App'x 684 (9th Cir. 2008).

Although Plaintiffs' causation experts, Drs. Weisenburger and Shustov, are unquestionably qualified in their respective fields, neither is "proposing to testify about matters growing naturally and directly out of research [he has] conducted independent of the litigation"; they have instead "developed their opinions expressly for purposes of testifying." *Daubert v. Merrell Dow Pharm., Inc.*, 43 F.3d 1311, 1317 (9th Cir. 1995) ("*Daubert II*"); *see also, e.g.*, *Clausen v. M/V New Carissa*, 339 F.3d 1049, 1056 (9th Cir. 2003) (same). Weisenburger is a leader in the field of hematopathology, the diagnosis of diseases of the blood, and has published "hundreds of papers" on lymphomas, including T-cell lymphomas. Ex. 4 at 20:5-17. Yet he has never authored a scientific paper identifying—or even hypothesizing—TNF inhibitors or thiopurines as a cause of lymphoma and, accordingly, admitted that his opinions in this case were developed solely for this litigation. *Id*. at 20-21. Weisenburger candidly conceded that his opinions here do not meet the "more rigorous" standard of medical certainty he applies when writing his medical-scientific articles. *Id*. at 118-19.

While Shustov has treated several cases of HSTCL and actively researched *treatments* for the disease, Ex. 6. at 22, 69, he is ill-equipped to opine on causation. He has never done any independent research or authored a publication on the topic of the etiology or causes of cancer. *Id.* at 28. Not surprisingly, Shustov has never expressed in an official statement or publication outside this litigation that thiopurines or anti-TNFs, either alone or in combination, "cause or contribute to the development of HSTCL," *id*. at 74, nor would he be "comfortable publishing that information right now." *Id*. at 75. Indeed, in contrast to his opinions in this litigation, he is careful to avoid leaping to causal determinations in his clinical practice. Shustov has treated two HSTCL patients who, like Wendell, were young males with a long history of IBD who were treated with both a thiopurine and anti-TNF therapy. *Id*. at 23. But while Shustov insists that he is able to identify 6-MP, Remicade, and Humira as causes of Wendell's HSTCL (despite never having treated him) simply by "work[ing] backwards" from the fact that he developed HSTCL after using these therapies, *id*. 189-90, he disclaims any determination that his own patients' HSTCL was caused by the same therapy, *id*. at 202-03.

Weisenburger's and Shustov's causation opinions are precisely the type of made-for-litigation opinions that careful *Daubert* scrutiny is designed to exclude. Plaintiffs cannot avoid summary

judgment with experts, no matter how well-credentialed otherwise, who have no scientific or medical basis to opine that Defendants' medicines caused Wendell's HSTCL.

C. Plaintiffs Cannot Meet Their Burden To Demonstrate General Causation as to the Anti-TNF Defendants.

Plaintiffs' experts concede there is no scientific evidence to support the proposition that anti-TNF therapies in themselves can cause or contribute to HSTCL. They also admit that there is not one well-controlled scientific study demonstrating that adding anti-TNF therapy to a regimen of 6-MP increases a patient's risk of HSTCL. Accordingly, Plaintiffs fail to meet their burden to show that Remicade or Humira can cause or contribute to the development of HSTCL.

1. Plaintiffs' Experts Admit There Is No Evidence That Anti-TNF Therapies Alone Are Capable of Causing HSTCL.

It is undisputed that there is no scientific evidence that anti-TNF therapies themselves (i.e., as monotherapy) increase the risk of HSTCL. Weisenburger squarely admitted that there are "no epidemiologic studies demonstrating an association between anti-TNF monotherapy and HSTCL." Ex. 4 at 96. Thus, Weisenburger "do[es not] offer any opinion in this case as to the effects of anti-TNF monotherapy on either NHL generally or HSTCL specifically." *Id*. at 100. Likewise, Shustov could not even identify a single case report of HSTCL in an IBD patient who was on anti-TNF monotherapy, Ex. 6 at 107, nor did he reference any study showing that anti-TNF monotherapy increases the risk of developing HSTCL. *See generally id*.; Ex. 8 (Shustov Rep.).

2. Plaintiffs' Experts Admit There Is No Evidence That Adding Anti-TNF Therapy to a Thiopurine Regimen Causes HSTCL.

In the absence of any reliable evidence linking anti-TNF therapy to HSTCL, Plaintiffs' experts resort to their speculative "combination use" theory. Every case report plaintiffs' experts have cited of HSTCL in IBD patients taking anti-TNF therapy also involved use of thiopurines (and every such case report in a patient on Humira also involved use of Remicade and thiopurines). *See* Ex. 5 (Kotlyar 2011).[5] Shustov hypothesizes that although anti-TNFs alone do not increase the risk of HSTCL, "*[i]t is thought* that this drug combination *might* cause both DNA damage (purine analogue), leading to the

[5] For the reasons stated *infra* Section II.E, case reports are not valid scientific evidence of causation in the first place.

development of malignant or cancerous clones and immunosuppression (TNF-alpha inhibitors), that allows for a reduced immunologic surveillance for cancer." *Id*. at 12 (emphases added). Shustov admits that his speculation that combination therapy "might" operate in this fashion is merely a hypothesis of "biologic plausibility." Ex. 6 at 142-43. But he agrees that biological plausibility alone cannot prove causation. *See, e.g.*, *id*. at 63; *see also, e.g.*, *Henricksen*, 605 F. Supp. 2d at 1178 (hypotheses not admissible evidence). Because there is no evidence that anti-TNFs are themselves capable of causing HSTCL, this theory is inadequate in California as a matter of law. *See Avila*, 633 F.3d at 836.

Plaintiffs' experts admit that the hypothesis that "the combination of thiopurines and TNF antagonists further increases the risk of HSTCL over that of thiopurines alone," Ex. 8 (Shustov Rep.) at 12, has not been borne out by any scientific data. Weisenburger flatly acknowledged that "there's no conclusive data establishing that adding anti-TNFs to [a thiopurine] regimen increases the risk" of developing HSTCL. Ex. 4 at 106. Likewise, Shustov conceded that "no study has been able to control for the potential confounding effect of the combination" of anti-TNFs and thiopurines. Ex. 6 at 98. In fact, the only paper that even *purports* to compare combination therapy to thiopurine monotherapy, a 2013 paper published by Deepak et al.,[6] is one that Plaintiffs' experts admit "does not support the notion that adding anti-TNFs to a thiopurine regimen increases the risk of T-cell NHL." Ex. 4 (Weis. Dep.) at 214; *see also* Ex. 11 at 103, Table 5; Ex. 6 (Shustov Dep.) at 117.

D. Plaintiffs Cannot Meet Their Burden to Demonstrate Specific Causation as to the Anti-TNF Defendants.

As a threshold matter, the lack of evidence of general causation precludes Weisenburger or Shustov from offering a specific causation opinion that any of Defendants' therapies caused or contributed to Wendell's HSTCL. *See, e.g.*, *Redfoot v. B.F. Ascher & Co.*, 2007 WL 1593239, at *15 (N.D. Cal. June 1, 2007). Regardless, Plaintiffs cannot meet their burden of demonstrating specific causation because their experts applied no discernible methodology to determine the cause of Wendell's HSTCL, and because Plaintiffs' experts' own admissions contradict any allegation of causation here.

[6] Ex. 11 (Deepak, P., et al., T-Cell Non-Hodgkin's Lymphomas Reported to the FDA AERS With Tumor Necrosis Factor-Alpha (TNF-α) Inhibitors: Results of the REFURBISH Study, American Journal of Gastroenterology (2013), 99-105 ("Deepak 2013")). Deepak 2013 was published online in 2012, so it is occasionally referred to in the transcripts as "Deepak 2012."

1. Plaintiffs' Experts Applied No Discernible Methodology in Reaching Their Specific Causation Opinions.

When asked how he formed his specific causation opinion in this case, Shustov testified that he merely formed a judgment about whether he thought Wendell's medications were "related," "possibly related," or "not likely related" to his development of HSTCL based on his "knowledge of the medical literature, the knowledge of the patient, [and his] medical understanding and experience." Ex. 6 at 246:19-24. This is not a "methodology;" it is unreviewable expert fiat, and it is inadmissible under *Daubert*. *See e.g.*, *Dominique v. Holland Am. Line, N.V.*, 2013 WL 5437436, at *4 (W.D. Wash. Sept. 27, 2013) (excluding expert who "fail[ed] to show whether or how [he] used differential diagnosis" and did not "actually 'consider' alternative causes" or "offer any specifics to support the leap from general to specific causation").

Weisenburger's specific causation opinion is even more conclusory—he merely asserts that HSTCL typically occurs in young men with IBD on combination therapy and concludes that "[t]herefore" Wendell's use of combination therapy "caused or substantially contributed to the development of HSTCL." Ex. 7 (Weis. Rep.) at 2. In deposition he thus asserted "[i]t was probably all these drugs together in combination that resulted in the increased risk," but admitted that sorting out "what was etiologic and what wasn't" is "very difficult." Ex. 4 at 112:5-9. Like Shustov's *ipse dixit*, this conclusory assertion does not pass muster under *Daubert*. *See e.g.*, *Dominique*, 2013 WL 5437436, at *4.

The lack of any reliable methodology for ascribing specific causation here is underscored by the failure of either expert to account for the likelihood that Wendell's HSTCL resulted from an unknown cause, despite their testimony that at least 73% have no known cause. Where the majority of cases of a disease are idiopathic, courts often exclude causal opinions that fail to adequately account for the likelihood that the disease was caused by an unknown factor. *See, e.g.*, *Lopez v. Wyeth-Ayerst Labs.*, 1996 WL 784566, at *3 (N.D. Cal. Dec. 13, 1996) (Wilken, J.), *aff'd* 139 F.3d 905 (9th Cir. 1998) (failure to eliminate all other potential causes "particularly troubling" where 30-40% of cases idiopathic). Shustov admitted that it is "particularly difficult" to perform differential diagnosis where a majority of cases are idiopathic. Ex. 6 at 162.

In such situations, "analysis beyond a differential diagnosis is required." *Henricksen*, 605 F. Supp. 2d at 1162. Yet Plaintiffs' experts performed no such analysis. Shustov's testimony underscores the point: when he was asked whether there was anything in particular about Wendell's case that would allow him to say that Defendants' therapies, rather than some other risk factor, caused Wendell's HSTCL, Shustov replied: "Well, we have no idea what the risk factors are for de novo hepatosplenic T-cell lymphoma. We don't even know what to look for." Ex. 6 at 237. Likewise Weisenburger admitted that he could not rule out an unknown cause for Wendell's HSTCL and that he *assumed* the treatments were causal because they are, in his opinion, risk factors:

> Q. [I]n assessing the possible causes of Mr. Wendell's HSTCL did you consider the fact that Mr. Wendell's HSTCL might have been de novo?
>
> A. Yes.
>
> Q. And were you able to rule out that fact or that possibility?
>
> A. Not entirely, no. When you have a patient with obvious and known risk factors, you tend to assume that those risk factors were the cause.
>
> Q. Is that what you did in this case? Because he had obvious and known risk factors, you assumed those were the cause?
>
> A. Yes.

Ex. 4 at 113-14. But even assuming (beyond all evidence) that anti-TNF therapies might increase the risk of HSTCL in some patients, Plaintiffs' experts' attempt to ascribe causation here is an impermissible leap of logic: "[s]tanding alone, the presence of a known risk factor is not a sufficient basis for ruling out idiopathic origin in a particular case, particularly where most cases of the disease have no known cause." *Henricksen*, 605 F. Supp. 2d at 1162; *Lopez*, 1996 WL 784566 at *3.

2. Plaintiffs' Experts' Admissions Regarding Humira and Remicade Preclude a Showing of Specific Causation as to Those Therapies.

Plaintiffs' experts concede that they cannot even opine that anti-TNF therapy increased Wendell's risk of HSTCL, much less that the anti-TNF therapies were a but-for or concurrent independent cause of his HSTCL. Their opinions thus fall short of the requirements for establishing

causation under California law. First, neither Weisenburger nor Shustov could opine that Wendell would not have developed HSTCL but for his use of anti-TNF therapies. Shustov testified that he "wouldn't be able to answer that question," because he does not "know one way or the other." Ex. 6 at 165 (Humira), 234 (Remicade). Weisenburger likewise testified that "[w]e don't know the answer to that." Ex. 4 at 112:18-20. Plaintiffs thereffail to satisfy the default rule of Section 432, the 'but for' test of Section 432(1). *Viner*, 30 Cal. 4th at 1240.

Second, both experts conceded that they could not conclude that Wendell's anti-TNF therapies were concurrent independent causes of his HSTCL under Section 432(2). Weisenburger, for example, testified that it was "unlikely" that "Wendell [would] have developed HSTCL if he had only taken Humira as a monotherapy." Ex. 4 at 113. Shustov could not even opine that Humira increased Wendell's risk of HSTCL beyond the risk he already had, let alone that it was sufficient to cause his disease. Ex. 6 at 165-66. Plaintiffs therefore fail to satisfy the "concurrent independent cause" exception of Section 432(2).

In the end, neither Weisenburger nor Shustov could say that taking anti-TNF therapies had *any* contribution to Wendell's risk of HSTCL. As Weisenburger flatly admitted, "*it would be impossible*, based on the data that we have today, *to say whether or not the addition of Humira to Max[x] Wendell's treatment regimen increased his risk of HSTCL*." Ex. 4 at 217 (emphasis added). The same true for Remicade. *Id*. Shustov likewise could not identify *any* contribution by these therapies to the HSTCL risk:

> Q. Can you tell me what the relative risk of each of those medicines [6-MP, Remicade, and Humira] was to the contribution of HSTCL development?
>
> A. I cannot quantify that.
>
> Q. Okay. And can you separate out for me the relative contribution of Humira to that…risk.
>
> A. I cannot.

Ex. 6 at 164-65.

3. Plaintiffs Cannot Show That Humira Caused Wendell's HSTCL Given the Short Duration of Use Immediately Before Diagnosis.

Plaintiffs' claims against Abbott fail for another reason: Wendell took Humira for only a few months, immediately before he developed HSTCL, and there is no evidence that this short use of that medication contributed to the development of HSTCL. Shustov squarely admitted that he is aware of no "data to suggest that being on an anti-TNF treatment in combination with thiopurines for seven months increases the risk for HSTCL." Ex. 6 at 156. And in Weisenburger's opinion, "eight months would be an extremely short latency period for NHL." Ex. 4 at 57. Indeed, Shustov testified that he could not even say one way or the other whether Wendell already had HSTCL at the time he started taking Humira. Ex. 6 at 158, 160. Plaintiffs thus have no evidence from which a jury could do anything but impermissibly speculate that Wendell's use of Humira for seven months immediately before he developed HSTCL caused or contributed to his development of the cancer. *See, e.g.*, *Claar v. Burlington N. R. Co.*, 29 F.3d 499, 502 (9th Cir. 1994).

E. Plaintiffs Cannot Establish That Purinethol Was a Substantial Factor in Causing Maxx Wendell's HSTCL.

1. Plaintiffs' Causation Experts' Testimony Should Be Excluded.

Scientists (and courts) agree, and Plaintiffs' causation experts admit, case reports and case series cannot establish causation. General causation must be established through evidence "'derived by the scientific method' and 'based on scientifically valid principles.'" *Jones v. United States*, 933 F. Supp. 894, 897 (N.D. Cal. 1996) (quoting *Daubert I* and entering judgment for defendants after finding expert causation testimony inadmissible), *aff'd*, 127 F.3d 1154 (9th Cir. 1997) . It cannot be established on the basis of "anecdotal case reports, reviews of research done by other people, or studies lacking a control group" because such evidence is "not derived through the scientific method." *Id*. at 899. "[C]ase reports are not reliable scientific evidence of causation…." *Casey v. Ohio Med. Prods.*, 877 F. Supp. 1380, 1385 (N.D. Cal. 1995). Accordingly, case reports "do not rise to the level of scientific reliability, methodology or validation required by *Daubert*." *Id*.; *see also Lopez v. Wyeth-Ayerst Labs.*, No. 94-4054-CW, 1996 WL 784566, at *4 (N.D. Cal. Dec. 13, 1996) ("Generally, courts have excluded expert causation testimony that is based upon such anecdotal or case reports."). Plaintiffs' own experts agree. *See* Ex. 6 (Shustov Dep.) at 68-69 ("where you're looking at whether particular treatments caused

HSTCL,…[c]ase reports can't establish causation"); Ex. 4 (Weis. Dep.) at 62-63 (causal judgments "should not be based on case reports alone").

Plaintiffs' experts have agreed that case reports are particularly suspect when they involve more than one potential cause: "when multiple exposures are associated with one another and also associated with a disease, it can be very difficult to analyze which, if any, of those exposures is actually causing the disease." Ex. 4 at 70; Ex. 6 at 67 (association between an exposure and a disease might be due to "confounding with some other causal exposure"). Case reports do not permit such an analysis because they "do not isolate and exclude potentially alternative causes." *Casey*, 877 F. Supp. at 1385. Thus, case reports of HSTCL in IBD patients treated with thiopurines alone or with anti-TNF therapies cannot establish causation in this case, because they do not isolate and exclude potentially alternative causes of the patients' HSTCL, including the various medications they are on, their underlying inflammatory disease, another underlying condition, or unknown causes.

Yet case reports and case series constitute the foundation of Plaintiffs' causation experts' opinions. The only study cited by Shustov in his report was *A Systematic Review of Factors That Contribute to Hepatosplenic T-Cell Lymphoma in Patients With Inflammatory Bowel Disease*, Clinical Gastroenterology and Hepatology (2011), by Kotlyar, D.S., et al., Vol. 9, 36-41 ("Kotlyar 2011"). Shustov cannot speak to the "statistical validity" of Kotlyar 2011. Ex. 6 at 181. Kotlyar 2011 is based on a review of reports in the FDA's MedWatch reporting system and case reports published in the literature, in other words, case reports. *See* Ex. 5 (Kotlyar 2011), at 36. It is not a cohort study or a case-control study. *See* Declaration of Robert J. Valuck, Ph.D, R.Ph. ("Valuck Decl.") ¶ 22. It provides no reliable basis for calculating risk. *Id*. at ¶¶ 22-23. Weisenburger admits that the Kotlyar paper "looked at cases" but was unable to control for confounding factors. Ex. 4 at 73. As a matter of law under *Daubert*, Kotlyar 2011 cannot provide a basis for general causation opinions in this action.

The other article relied upon by Plaintiffs' causation experts for their opinions that use of Purinethol can increase a patient's risk of developing HSTCL is Deepak 2013. Ex. 4 at 122-24; Ex. 6 at 178-185. Deepak 2013 is a case series that does not control for confounding factors. *See* Ex. 4 at 155-156. It does not calculate relative risk. *See* Valuck Decl., ¶ 21. It is not, and does not claim to be, a case-control study that can be used to calculate an odds ratio. *Id*. at ¶¶ 25-26.

Scientists—including Plaintiffs' experts—agree that "[e]pidemiologic studies in humans provide the best and most convincing data linking environmental exposures to cancer." Ex. 4 at 61; *see also Lopez*, 1996 WL 784566, at *3 ("Epidemiological evidence is one of the most valuable pieces of scientific evidence of causation."). Properly designed and performed epidemiological studies can be used to establish statistically significant association. *See* Valuck Decl., ¶ 10. If such an association is found, the epidemiologist applies "well accepted" epidemiologic criteria known as the Bradford Hill criteria to decide whether an association is actually causal. Ex. 4 at 68; Ex. 6 at 94.

There is no reliable scientific evidence to support either a statistically significant association or a causal link between consumption of 6-MP and HSTCL. There are no epidemiological studies finding an increased risk of HSTCL in IBD patients taking 6-MP alone or in combination with anti-TNFs. The consensus in the scientific community is that nobody knows what causes HSTCL or contributes to cause it. There are no scientifically established risk factors for HSTCL. *See* Valuck Decl., ¶ 17; Declaration of Andrew Place, M.D., Ph.D., ¶ 6. There are only case reports and hypotheses. *See* Valuck Decl., ¶¶ 20-21.

The mechanisms by which HSTCL is initiated and develops also are unknown. *See* Place Decl., ¶ 6. Nevertheless, Plaintiffs' experts have attempted to buttress their reliance upon case reports by pointing to what they characterize as "biologically plausible mechanisms." Shustov acknowledges, however, that biologic plausibility is a hypothesis and that his hypothetical mechanism for 6-MP and HSTCL has not been tested. Ex. 6 at 62, 145-46, 190-91. He also agrees that biological plausibility alone cannot prove causation. *Id*. at 63. Further evidence of the hypothetical nature of the biologically plausible mechanisms proposed by Plaintiffs' experts is that they cannot agree on the role played by one of the hypothesized mechanisms attributed to 6-MP by Weisenburger—immunosuppression. *Compare* Ex. 6 at 227 *with* Ex. 4 at 158-60. Their inability to reach an agreement on that purported mechanism is not surprising. Evidence of immunosuppression is absent from 70 to 80% of the reported HSTCL cases. *See* Valuck Decl., ¶ 17; Place Decl., ¶ 17. Like other untested hypotheses, neither science nor the law allow Plaintiffs' experts to rely on hypothetical mechanisms to prove causation. *See, e.g.*, *Henricksen* 605 F. Supp. 2d 1178 (hypothesis is not admissible evidence); Place Decl., ¶ 19.

Lacking any valid scientific evidence, and possessing only articles about case reports, Plaintiffs' experts attempt to rely on data from studies about other lymphomas. They also attempt to rely upon chemical analogies. However, it is not proper scientific methodology to use data from studies regarding other lymphomas and to draw inferences or conclusions about HSTCL, a unique lymphoma. *See* Place Decl., ¶ 17; Valuck Decl., ¶¶ 33-35. Weisenburger admits this is true. Ex. 4 at 97-98. Yet the other studies expressly cited by Weisenburger concern, or derive, data from studies and articles about lymphomas in general, not HSTCL and include data about another thiopurine, azathioprine. *See* Ex. 7 at 3; Valuck Decl., ¶¶ 34-35. Not only is that improper from a scientific standpoint, *see* Valuck Decl., ¶¶ 33, but also it is improper legally. *See, e.g., Siharath v. Sandoz Pharms. Corp*., 131 F. Supp. 2d 1347, 1365 (N.D. Ga. 2001). The Court has held that it is the specific risk of HSTCL, and not the risk of other lymphomas, that is at issue in this case. *See* July 25, 2012 Order ("Order Granting Summary Judgment for GSK") (Dkt. 232) at 16-17.

Plaintiffs' experts attempt to rely upon chemical analogy—azathioprine—data presents another problem for them. It is not proper scientific methodology to rely upon chemical analogies absent proof from scientific studies that their effects are equal. Both Plaintiffs' experts admit azathioprine and 6-MP act differently in the body. *See* Ex. 4 at 176-178; Ex. 6 at 199-202. And, courts have recognized it is improper to attempt to prove general causation by using chemical analogies. *See, e.g., Schudel v. General Elec. Co.,* 120 F.3d 991, 996-97 (9th Cir.1997); *Siharath*, 131 F. Supp. 2d at 1363-64.

For these reasons, as well as the reasons set forth supra in Section II.B, the general causation opinions of Plaintiffs' experts with respect to 6-MP and HSTCL should be excluded.

As to specific causation, as with the anti-TNF therapies, the lack of evidence of general causation precludes Weisenburger or Shustov from offering a specific causation opinion that any of Defendants' therapies caused or contributed to Wendell's HSTCL. *See, e.g.*, *Redfoot v. B.F. Ascher & Co.*, 2007 WL 1593239, at *15 (N.D. Cal. June 1, 2007). In addition, Plaintiffs cannot meet their burden of demonstrating specific causation because their experts applied no discernible methodology to determine the cause of Wendell's HSTCL, and because Plaintiffs' experts' own admissions contradict any allegation of causation in Wendell's case.

As described in Section II.D.1, *supra*, there is no evidence here that Plaintiffs' experts performed a differential diagnosis—or employed any other discernible methodology—to determine the cause of Wendell's HSTCL. Moreover, among the potential causes that Shustov and Weisenburger cannot eliminate are severity of IBD as a cause of HSTCL and an underlying genetic defect or other underlying condition that caused both severe IBD and HSTCL in Wendell. *See* Place Decl., ¶ 14. Neither Shustov nor Weisenburger could identify any differences in disease course or presentation between HSTCL patients who had been exposed to IBD therapies and those HSTCL patients who had not. *See* Ex. 4 at 174-75; Ex. 6 at 196. The inability of Shustov and Weisenburger to eliminate those potential causes is particularly problematic and provides additional grounds for the exclusion of their causation opinions because they have testified that 73% of the reported cases of HSTCL are *de novo* and idiopathic. *See, e.g.*, *Lopez*, 1996 WL 784566, at *3 (failure to eliminate all other potential causes "particularly troubling" where 30-40% of cases idiopathic); *Henricksen*, 605 F. Supp. 2d at 1162 (rejecting differential diagnosis where 80-90% of cases idiopathic). Shustov admitted that it is "particularly difficult" to perform differential diagnosis where a majority of cases are idiopathic. Ex. 6 at 162. No differential diagnosis was done here, let alone the "analysis beyond a differential diagnosis…required" in such circumstances. *Henricksen*, 605 F. Supp. 2d at 1162.

Weisenburger described his "methodology" for determining causation with a rare disease as using "whatever data you have at hand. You try to consider that data and use your best judgment." Ex. 4 at 155-156. Weisenburger admits that case series and case reports are hypothesis generating, but then asserts, apparently for purposes of this case, they "can be used to kind of support one's overall conclusions." *Id*. at 64-65. Similarly, Shustov testified that because there is no evidence from proper scientific studies, "you default back to lower level of evidence that you have and if it doesn't exist, you go to the best clinical judgment and biological plausibility." Ex. 6 at 73. Neither expert would publish his opinions in this case. Ex. 4 at 118-19; Ex. 6 at 75. Those "methodologies" are not proper for general or specific causation. Because neither expert employed the kind of methodology (or really any methodology) required for their opinions to be admissible under FRE 702 and *Daubert*, their opinions with respect to Purinethol/6-MP must be excluded.

2. Plaintiffs Cannot Prove Causation.

Plaintiffs' claims against Teva are barred because Plaintiffs cannot prove that Wendell's use of Purinethol was a substantial factor causing his HSTCL. First, as demonstrated above, Plaintiffs' causation experts should be excluded and, therefore, Plaintiffs cannot meet their burden of proving general and specific causation as to Teva "within a reasonable medical probability based upon competent expert testimony." *Avila v. Willits Envtl. Remediation Trust*, 633 F.3d 828, 836 (9th Cir. 2011); *see also Jones v. Ortho Pharm. Corp.*, 163 Cal. App. 3d 396, 402 (1985). Second, Plaintiffs' claims in this case are based on the assertion that it was the combination of 6-MP and anti-TNF therapies that caused Wendell's HSTCL. And Plaintiffs' expert, Dr. Shustov, admitted that he could not quantify the contribution of any of the medicines taken by Maxx Wendell to his HSTCL. Ex. 6 at 164-65. For the reasons set forth *supra* in Section II.A, Plaintiffs cannot proceed on their combination therapy claim against Teva and summary judgment is appropriate for Teva.

III. PLAINTIFFS CANNOT ESTABLISH FAILURE TO WARN

A. Legal Standards Applicable to Failure-to-Warn Claims

Under California law, product liability claims for personal injury from taking a prescription drug are failure to warn claims. *See Brown v. Super. Ct.*, 44 Cal. 3d 1049, 1061 (Cal. 1988) ("comment k would impose liability on a drug manufacturer only if it failed to warn of a defect of which it either knew or should have known"). A duty to warn of a risk associated with a medicine is triggered when the risk was "actually known or reasonably scientifically knowable to the manufacturer." *See Carlin v. Super. Ct.*, 13 Cal. 4th 1104, 1117 (1996). The California Supreme Court has cautioned against imposing an affirmative duty to warn of every "possible risk, no matter how speculative, conjectural, or tentative," as doing so "inevitably dilut[es] the force of any specific warning given." *Finn v. G.D. Searle & Co.*, 35 Cal. 3d 691, 696, 701 (1984). "The strength of the causal link is thus relevant both to the issue of whether a warning should be given at all, and, if one is required, what form it should take." *Id*. The manufacturer's duty to warn runs to the prescribing physician, not to the consumer. *Carlin*, 13 Cal. 4th at 1116. Accordingly, "a product defect claim based on insufficient warnings cannot survive summary judgment if stronger warnings would not have altered the conduct of the prescribing physician." *Motus*, 358 F.3d at 661. Plaintiffs cannot prove proximate cause where the prescribing

physician did not read or rely upon a defendant's allegedly inadequate warnings. *See Conte v. Wyeth, Inc.*, 168 Cal. App. 4th 89, 112 (2009); *see also Motus v. Pfizer, Inc.*, 196 F. Supp. 2d 984, 996 (C.D. Cal. 2001), *aff'd*, 358 F.3d 659 (9th Cir. 2004)).

To carry the burden on their failure-to-warn claims, Plaintiffs must offer admissible expert testimony that the warning at issue was inadequate. *See, e.g.*, *Salinas v. Amteck of Ky., Inc.*, 682 F. Supp. 2d 1022, 1031 (N.D. Cal. 2010) (granting summary judgment where plaintiffs failed to rebut defendants' experts' testimony that product warnings met regulatory standards); *N. Trust Co. v. Upjohn Co.*, 213 Ill. App. 3d 390, 398 (1991) (collecting cases requiring expert testimony on claims for failure to warn).

In this case Dr. Rich prescribed each of Defendants' products as therapies for IBD "off label"—*i.e.,* for a use not approved by FDA. Off-label use is a widespread, legitimate, and accepted practice among doctors, but a drug manufacturer is only liable for a failure to warn in connection with an off-label use if it promoted that use. *Huntman v. Danek Med., Inc.*, 1998 WL 663362, at *6 (S.D. Cal. July 24, 1998) ("In the absence of evidence that a doctor made the decision to use a product in an 'off-label' manner in reliance on a manufacturer's misrepresentations, claims for failure to warn…cannot stand."). Mere knowledge of "off-label" use is insufficient. *See Cox v. Depuy Motech, Inc.*, 2000 WL 1160486 (S.D. Cal. Mar. 29, 2000). This Court previously recognized the *Huntman* rule in its ruling on Abbott's earlier motion to dismiss. *See* January 20, 2010 Order (Dkt 98). The Court allowed Plaintiffs' negligence and strict liability failure-to-warn claims against Abbott to go forward *at the pleading stage* only because Plaintiffs had "at least in a general fashion, alleged that Abbott Labs promoted the off-label use of Hum[i]ra." *Id*. at 5.

B. Plaintiffs Cannot Prove Their Failure to Warn Claim Against Teva.

Plaintiffs cannot establish their failure to warn claim against Defendant for six independent reasons, any one of which is sufficient grounds for granting summary judgment in Teva's favor.

First, because Wendell's use of Purinethol was "off-label," Plaintiffs' failure-to-warn claims against Teva "cannot stand" without proof that Teva promoted the off-label use and that Dr. Rich relied on that off-label promotion. *Huntman*, 1998 WL 663362, at *6. There is no evidence of off-label promotion here. This Court previously recognized the *Huntman* rule in its ruling on Abbott's earlier

motion to dismiss Plaintiff's complaint. *See* January 20, 2010 Order (Dkt 98). The Court allowed Plaintiffs' negligence and strict liability failure-to-warn claims against Abbott to go forward *at the pleading stage* because Plaintiffs had "at least in a general fashion, alleged that Abbott Labs promoted the off-label use of Hum[i]ra." *Id*. at 5. Plaintiffs alleged in their complaint that Teva promoted the "off-label" use of Purinethol. FAC (Dkt. 165) ¶ 49. Discovery has closed, however, and it is now clear that Plaintiffs have no evidence of either off-label promotion by Teva or reliance by Dr. Rich on any statements by Teva. It is undisputed that Dr. Rich decided to prescribe 6-MP to treat Maxx Wendell based on information he learned during his fellowship, as well as on information he obtained from reading medical articles, from speaking with other professionals in his field, and from "patient experience." Ex. 1 (Rich Dep.) at 274-75. He learned about the use of 6-MP in pediatric patients with IBD during his pediatric gastroenterology fellowship training, which lasted from 1989 to 1992. *Id*. at 84, 37-38. This is well before he treated Maxx Wendell, and many years before Maxx Wendell had a prescription filled with Teva's Purinethol, which occurred only between December 16, 2003, and July 27, 2004. Ex. 13 (Plaintiffs' pharmacy records) at 7-12. Teva is therefore entitled to summary judgment under *Huntman*. 1998 WL 663362, at *6.

Second, Dr. Rich never read Teva's labeling, so any purportedly inadequate warning could not have been the proximate cause of Plaintiffs' alleged injuries. As noted above, Dr. Rich's sources of information about 6-MP were his fellowship training, medical articles, other professionals in his field, and "patient experience." Ex. 1 (Rich Dep.) at 274-275. It is not Dr. Rich's regular practice to look at drug labeling and he had no recollection of reading anything about Purinethol written, published, or disseminated by Teva (*id*. at 192, 283) or of ever being visited by a representative from Teva with regard to Purinethol (*id*. at 20). Because Dr. Rich never reviewed or relied on Teva's labeling for Purinethol, any alleged deficiency in the labeling cannot be the proximate cause of Plaintiffs' alleged injuries. *See Motus*, 358 F.3d at 661; *see also Conte*, 168 Cal. App. 4th at 112. Teva should be dismissed from this case for that reason.

Third, Plaintiffs regulatory expert, Dr. David Ross, opines that Teva should have warned of HSTCL risk in 2006, but Wendell's last prescription for Teva's Purinethol was filled on July 27, 2004. In his report, Ross offers the following opinion specific to Purinethol:

> 3. Purinethol
>
> The labeling for Purinethol (mercaptopurine) should have been updated and the product's manufacturer, Teva, should have alerted physicians at the same time that the Remicade label was changed to reflect the information about HSTCL cases, but certainly no later than mid-2006. In fact, Teva did not add a warning to the label for Purinethol until 2011, and then only after being ordered to by the FDA.

Ex. 12 (Ross Rep.) at 5. As Ross acknowledges, the label for Remicade was changed to incorporate information about HSTCL cases on May 19, 2006. *Id*. at 51. Thus Ross's opinion specific to Purinethol is that the label for the product should have been updated in May 2006. Putting aside for the moment why that opinion is erroneous, the opinion, even if considered, does not allow Plaintiffs to proceed against Teva.[7] Wendell last had a prescription filled with a Teva product earlier on July 27, 2004. Ex. 13 (Plaintiffs' pharmacy records) at 12. Between July 27, 2004, and March 12, 2007, Maxx Wendell filled prescriptions for 6-MP with a generic product distributed by a competitor, Par Pharmaceutical, Inc., rather than Teva's Purinethol. *Id*. at 2-13. Plaintiffs' own expert places the date for an HSTCL warning on Purinethol approximately two years after Wendell's last prescription filled with Teva's product. Plaintiffs cannot cite any cases holding that a manufacturer of a brand drug may be held liable in product liability under California law for personal injuries allegedly sustained by ingestion of a generic drug sold by another company. Rather, California follows the well-accepted legal principle that "a manufacturer owes no duty to consumers injured by a competitor's product." *Conte*, 168 Cal. App. 4th at 106 n.13. Teva should be dismissed from the case for this reason.

Fourth, Teva had no duty to warn during the period when Wendell used Purinethol because there had been no cases of HSTCL reported in patients on Purinethol at that time Wendell had prescriptions filled with Teva's Purinethol for eight months, from December 16, 2003, to July 27, 2004. GSK was dismissed from this action because the Court determined that, as of July 1, 2003, when GSK sold Purinethol to Teva, there was insufficient evidence for a reasonable jury to decide that GSK had a duty to warn of the risk of HSTCL. *See* Order Granting Summary Judgment for GSK (Dkt. 232) at 27. The Court's holding, based upon the absence of reports in the scientific literature of HSTCL in patients

[7] Teva reserves its right to later move for exclusion of Dr. Ross's opinions, if necessary.

taking Purinethol for IBD, is equally applicable to Teva. There were no reports published in the medical literature between July 1, 2003, and July 27, 2004 of HSTCL in patients taking Purinethol. Plaintiffs have adduced no evidence to the contrary, nor can they. Indeed, Ross admits there were no reports in the medical literature as of July 27, 2004, concerning HSTCL diagnosed in a patient treated with Purinethol. Ex. 15 (Ross Dep. II) at 328. Ross also admits that no report of HSTCL in a patient treated with Purinethol was received by Teva as of July 27, 2004. *See* Ex. 10 (Ross Dep. I) at 308. As was true for GSK with respect to time periods preceding July 1, 2003, Teva had no duty to warn of a risk of HSTCL before July 27, 2004, because there was no evidence of such a risk at that time. Teva should be dismissed from this action.

Fifth, Ross opines that Teva should have changed its labeling to warn about HSTCL when the boxed warning regarding HSTCL was added to the label for Remicade in May of 2006. Ex. 12 (Ross Rep.) at 5. Again, this time period is after Wendell stopped taking Teva's Purinethol. However, even if periods after July 27, 2004, were to be considered, summary judgment for Teva is proper. Dr. Rich was aware of the information contained in the boxed warning for Remicade before the warning was added and also received a "Dear Doctor" letter alerting him to the boxed warning. Ex. 1 (Rich Dep.) at 201-02. That boxed warning advised physicians there had been reports of HSTCL is patients taking 6-MP. Ex. 12 (Ross Rep.) at 51. Accordingly, even had Teva been aware of the boxed warning for Remicade in May 2006, any alleged failure to change the labeling for Purinethol to provide Dr. Rich with information he already possessed cannot be the proximate cause of Plaintiffs' injury. "There is no requirement that a manufacturer must give a warning which could not possibly be effective in lessening the plaintiff's risk of harm." *Rosburg v. Minn. Mining & Mfg. Co.*, 181 Cal. App. 3d 726, 735 (1986). Teva should be dismissed from this action.

Sixth, Plaintiffs must prove that an alleged failure to warn by Teva was the proximate cause of their injuries. *See, e.g., Ramirez v. Plough, Inc.*, 6 Cal. 4th 539, 556 (1993); *see also Plummer v. Lederle Labs., Div. of Am. Cyanamid Co.*, 819 F.2d 349, 358 (2d Cir. 1987) (applying California law, relied on by the Ninth Circuit in *Motus v. Pfizer, Inc.*, 358 F.3d 659 (9th Cir. 2004). Teva has moved for the exclusion of Plaintiffs' causation experts, Drs. Weisenburger and Shustov, *supra* Section II.E.1. However, even if permitted to testify, neither doctor can render an opinion as to when Wendell

developed HSTCL. *See, e.g.*, Ex. 4 (Weis. Dep.) at 112; Ex. 6 (Shustov Dep.) at 158. Even if periods after Teva's Purinethol was last dispensed on July 27, 2004, were considered, neither expert can opine that if Teva had changed the labeling for Purinethol in May 2006 to include information about HSTCL cases (as Ross asserts) that Maxx Wendell would not have developed HSTCL. In fact, Dr. Shustov testified that he cannot rule out that Maxx Wendell already had HSTCL at the time Teva acquired Purinethol from GSK in July 2003. *Id*. at 223. Consequently, as a matter of law, Plaintiffs cannot prove that it is more likely than not that any purported failure to warn on the part of Teva caused Plaintiffs' alleged injuries. Plaintiffs' failure to warn claims against Teva should be dismissed for that reason as well.

C. Abbott Did Not Have or Breach any Duty to Warn.

1. Abbott Had No Duty to Warn About Risks Associated with Wendell's Off-Label Use of Humira.

As with Teva, Plaintiffs' failure-to-warn claims against Abbott fail under *Huntman* because Dr. Rich prescribed Humira for an off-label use that was not approved by the FDA or recommended by Abbott. *Huntman*, 1998 WL 663362, at *6. In allowing Plaintiffs' failure-to-warn claims to go forward at the pleading stage, the Court pointedly cautioned Plaintiffs that "if it were later to appear that Plaintiffs had no good faith reason to believe that Abbott Labs promoted the off-label use of Humira, Rule 11 sanctions would apply." January 20, 2010 Order (Dkt 98) at 6 n.4. Such general pleading is no longer enough. Plaintiffs have had four years to discover evidence of off-label promotion by Abbott for Wendell's condition. Plaintiffs have uncovered no evidence that Abbott promoted off-label use of Humira for the treatment of IBD, let alone that Dr. Rich relied on any statement by Abbott in prescribing Humira off-label for the treatment of Wendell's ulcerative colitis. *See generally* Ex. 1 (Rich Dep.). Abbott is thus entitled to summary judgment on Plaintiffs' failure-to-warn claims.

2. Abbott Had No Duty to Warn Where It Had Not Received a Single Report of HSTCL in Patients Like Wendell.

Abbott also did not breach any duty to warn here for the independent reason that, as to Humira, the potential risk of HSTCL was not one that was "known or knowable in light of the generally recognized and prevailing best scientific and medical knowledge available at the time of manufacture

and distribution." *Carlin*, 13 Cal. 4th at 1112. It is undisputed that at the time Wendell used Humira,[8] there was not a single reported case of HSTCL in IBD patients who had taken Humira. Ex. 10 (Ross Dep. I) at 212, 214. Because Abbott had no reported HSTCL cases at the time of Wendell's prescription, the risk of HSTCL was nothing more than a theoretical hazard—not a risk that was "*actually known or reasonably scientifically knowable*." *Carlin*, 13 Cal. 14th at 1112. Accordingly, Abbott had no duty to to warn. *See id*.; July 25, 2012 Order (Dkt. 232) at 26 (holding that GSK could not be held liable for failure-to-warn where "information concerning the occurrence of hepatosplenic T-cell lymphoma in connection with Purinethol was not reported to AERS or discussed in the medical literature until after GSK ceased to distribute the drug").

Ross's contention that Abbott should have added an HSTCL warning to the *Humira* label when it learned of rare HSTCL cases in patients who had taken *Remicade* is not supported by any facts, data, or industry/regulatory practice. Ex. 10 at 223-24. Ross admitted that he is not aware of a single FDA regulation or any other guidance or authority to support the notion that rare cases of a disease involving one drug give rise to a duty to warn of that disease involving another drug. *Id*. at 231, 232, 233-34. To the contrary, he admitted that the FDA's general approach to evaluating the safety of similar drugs is based on *data*, not *assumptions* that the risks will be the same: "[W]here the *data* [regarding adverse events] is similar, especially where there is a biologic rationale, class labeling may be warranted, but where the *data* differ, different language may be appropriate for different agents." *Id*. at 267 (emphases added).

Ross cites no such data to support his speculation that "a risk related to Remicade is highly likely to also arise with Humira," Ex. 12 (Ross Rep.) at 6, *see generally* Exs. 10 and 15, and Ross would be unqualified to put forward any such opinion in any event. Ex. 10 at 295 (conceding he is "not offering an opinion regarding the mechanisms of action of Humira and Remicade on the basis of any specialized training in pharmacology or toxicology or immunology"); *id*. at 294 (admitting he cited no references regarding similarities between Remicade and Humira in his report). He does not claim expertise in

[8] Evidence that post-dates Wendell's prescription is irrelevant to the *Carlin* inquiry. *See Carlin*, 13 Cal. 4th at 1113 n.3 (1996) ("the knowledge element must exist at the time of distribution…. Obviously, subsequently developed scientific data would not be controlling.").

pharmacokinetics, and he has done nothing to analyze whether the drugs have different risk profiles or whether those differences may reflect a different risk relating to HSTCL.

"[N]othing in either *Daubert* or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert." *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997); *see also* Fed. R. Evid. 702 advisory committee notes (2000 amendments) ("The trial court's gatekeeping function requires more than simply 'taking the expert's word for it.'" (quoting *Daubert II*)). Ross's unsupported *ipse dixit* opinion that the general similarities between Remicade and Humira are sufficient to require a Humira HSTCL warning on the basis of cases only in patients who had taken Remicade is inadmissible under *Daubert* and therefore cannot support Plaintiffs' argument that Abbott had a duty to warn about HSTCL in May 2006.

D. Plaintiffs Failed To Establish that Centocor Breached Any Duty to Warn.

1. Centocor Had No Duty to Warn About Risks Associated with Wendell's Off-Label Use of Remicade.

As with Teva and Abbott, Plaintiffs' failure-to-warn claims against Centocor fail under *Huntman* because Dr. Rich elected to prescribe Remicade for an off-label use that was not approved by the FDA or recommended by Centocor. *See Supra* Sections III.B, III.C.1. Plaintiffs have no evidence that Centocor promoted off-label use of Remicade for the treatment of IBD, let alone that Dr. Rich relied on any statement by Centocor regarding use of Remicade off-label.

2. Plaintiffs' Failure-to-Warn Case Against Centocor is Based on Inadmissible Ipse Dixit Testimony.

Plaintiffs' failure-to-warn claims against Centocor fail for the independent reason that Plaintiffs' warnings expert cannot produce an admissible opinion supporting a finding that a risk of HSTCL was "known or knowable in light of the generally recognized and prevailing best scientific and medical knowledge" before Wendell was treated with off-label combination therapy. *See Carlin*, 13 Cal. 4th at 1112. Ross, who has no formal training in oncology, and was not even aware that HSTCL existed until he was retained for this lawsuit, , is not qualified to assess the science at issue, nor did he consult an expert able to do so. Ex. 10 at 34, 146. His "say so" opinions are inadmissible and insufficient to avoid

summary judgment. *Joiner*, 522 U.S. at 146 ("the *ipse dixit* of the expert," does not rise above the level of speculation).

Ross's opinion that the Remicade labeling should have mentioned that reports of HSTCL had been received in 2002 (Cases 1 and 2), Ex. 10 (Ross Dep. I) at 130-131, 146, is based on a flawed premise. Centocor did not learn that either Case 1 or Case 2 was potentially a case of HSTCL until May 2006. As this Court has ruled, there is no duty to warn when no cases of a specific event have been reported. July 25, 2012 Order (Dkt. 232) at 26 (GSK not liable where "information concerning the occurrence of hepatosplenic T-cell lymphoma in connection with Purinethol was not reported to AERS or discussed in the medical literature until after GSK ceased to distribute the drug").

Ross asserts that Centocor should have sought additional data regarding Cases 1 and 2 from the reporters in 2002 to determine that they were cases of HSTCL, despite the fact that there had not been one single case of HSTCL reported in any patient who had taken Remicade at that time. *See* Ex. 10 at 146-47. Ross provides no authority to support his apparent assertion that Centocor should have anticipated HSTCL reports before they happened (essentially claiming that zero case reports constitutes a safety signal). Either way, Ross is wholly unqualified to render such opinion because it pertains to HSTCL, not regulations. He does not claim expertise in oncology, and has never studied HSTCL. Ex. 10 at 34, 146. Ross acknowledges more than 200 types of lymphomas have been identified and many are lethal and aggressive. *See* Ex. 10 at 109-110. He did not review the body of data available to Centocor at the time, *id*. at 112-13, he was not aware of what analysis was applied to that data, *id*. at 113, and when asked if he was offering an opinion as to how Centocor determined what types of information regarding lymphoma, if any, to seek, he said, "I don't have access to those reviews…or the raw data for that matter. So it is not possible for me to say, well, I think they should have done X. I mean, it's—I think without that information, it's really impossible for me to say." *Id*. at 114. Moreover, his premise that the reporting hospitals would have had an HSTCL diagnosis to provide for Case Report 1 and 2, if asked in 2002 and 2003, is speculative because Ross agreed medical data is not always available or obtainable. *Id*. at 59. For example, in Case 4, the only case in which the event reporter was deposed, the patient was diagnosed after a later second opinion. Ex. 20 (Baldassano Dep.) at 52-53.

Ross's speculation is insufficient to establish that a risk for HSTCL is "scientifically knowable" as intended by *Carlin*.

Adding Cases 3 and 4 to the analysis does not change the result. Both cases had possible alternative explanations for the event—concomitant medications that could contribute to the event and co-morbid medical conditions. These two reports do not raise a duty to warn. *See* Ex. 22 (3/2005 FDA Guidance) at 6-7 (stating that a valuable case report is one in which there is an "absence of alternative explanations for the event (e.g., no concomitant medications that could contribute to the event; no co-or pre-morbid medical conditions)"). Any opinion by Dr. Ross to the contrary would be unsupported *ipse dixit*. There is no duty to warn of every "possible risk, no matter how speculative, conjectural, or tentative," as doing so "inevitably dilut[es] the force of any specific warning given." *Finn v. G.D. Searle & Co.*, 35 Cal. 3d 691, 696, 701 (Cal. 1984). "The strength of the causal link is thus relevant both to the issue of whether a warning should be given at all, and, if one is required, what form it should take." *Id*.

Although Ross believes the 2004 warning preceding the 2006 HSTCL specific warning is inadequate, Ex. 10 at 117, he cannot articulate a basis for his opinion. FDA implemented class labeling for anti-TNF lymphoma warnings in 2004, so the agency controlled the specific warning language and the timing of its implementation. *See* Ex. 21 (10/4/2004 letter from Centocor to FDA) (referring to labeling drafted by FDA and agreed to by Centocor). Under these circumstances, second guessing FDA's decisions cannot raise questions of fact sufficient to defeat summary judgment. His opinions are demonstrably unreliable as he admittedly did not review the data accumulated by FDA or the information exchanged between FDA and Centocor about malignancies, lymphomas, and anti-TNF therapies. Ex. 10 (Ross Dep. I) at 18, 19-20, 85-86, 112-13, 118-19, 131. Moreover, Ross ignores important facts that FDA guidance documents say must be considered when evaluating adverse event reports for possible label changes. *See* Ex. 22. Ross's opinion that Centocor should have warned differently is unreliable and should be excluded. *Kumho*, 526 U.S. at 149.

CONCLUSION

For the foregoing reasons, Defendants respectfully request that the Court exclude the testimony of Weisenburger, Shustov, and Ross and grant summary judgment in Defendants' favor on all claims.

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Respectfully submitted,

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that all counsel of record who have consented to electronic service are being served with a copy of the attached **NOTICE OF MOTION AND MOTION FOR SUMMARY JUDGMENT BY DEFENDANTS ABBOTT LABORATORIES, JOHNSON & JOHNSON, CENTOCOR, INC., AND TEVA PHARMACEUTICALS USA, INC.; MEMORANDUM OF POINTS AND AUTHORITIES IN SUPPORT** via the CM/ECF system on January 9, 2014, and via overnight delivery (Federal Express) to the non-CM/ECF participants listed below.

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